EMARKS/ARGUMENTS

Claims 7-9, 12, 13, 17, 18, 20 and 23 are pending in this application. Claims 1-6, 10, 11, 14, 15, 16, 19, 21, 22 and 24 are cancelled without prejudice or disclaimer. Claims 7-9, 12, 13, 17, 18, 20 and 23 are rejected. Claims 7-9, 12, 13, 17, 18, 20 and 23 are hereby amended and new claims 24 -27 are hereby added. Support for amendment to independent claims 7, 9, 12 and 13 is found on page 11, lines 26-35. Support for new claims 24 - 27 is found in original claims 7, 9, 12 and 13. The amendments new claims do not introduce any new matter.

In consideration of the amendments and the following remarks, reconsideration of claims 7-9, 12, 13, 17, 18, 20 and 23, and consideration of new claims 24 -27 are respectfully requested.

Claim Rejections - 35 USC § 112, second paragraph

Claims 7-9, 12, 13, 17, 18, 20 and 23 under are rejected under 35 U.S.C. §112, second paragraph.

Claim 7 has been amended for clarity by replacing the recitation "double-domain recombinant AL2 gene encoding a modified transcription activator protein" with the recitation "isolated recombinant polynucleotide encoding a mutant Begomovirus transcription activator protein, wherein said recombinant polynucleotide is a modified open reading frame of a selected wild-type AL2 gene from a Begomovirus strain, and wherein said mutant Begomovirus transcription activator protein is a mutant form of a wild-type Begomovirus transcription activator protein expressed by the selected wild-type AL2 gene." It is believed that this amendment overcomes the rejection of claim 7 and its dependent claims as being unclear based on the terms "double-domain," "AL2," "gene," "modified" and "about." Claim 7 has also been amended to recite a "first mutation;" it is believed that this amendment overcomes the rejection of claims 7 and 8 as lacking antecedent basis.

The Patent Office has indicated that the frame of reference for the amino acid numbers recited in claim 7 is not clear. Figure 1 shows the amino acid sequences for several transcriptional activator proteins isolated from different Begomoviruses. These sequences correspond to SEQ. ID. NO:'s 1-13. As stated in the "Brief Description of the Figures," the

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sequen s are all aligned, oriented in the customary fashion starting with amino acid number 1 at the N-t minal end (located on the top left side of the page), and en ing with amino acid number 131 (lo ited at the C-terminal end on the lower right side of the p ge). Applicant respectfully submit that there is a frame of reference for the recited amin acid numbers; accordingly, Applic it respectfully requests withdrawal of this rejection.

laim 13 has been modified to replace the term "plurality" with the term "one or more." Applic it submits that this modification renders moot the rejection f claim 13 based on the term "plural y," and Applicant further submits that the amendment d s not constitute new matter given t common meaning of the term "plurality," which is "the s ate of being more than one," accordi g to Merriam Webster's Collegiate® Dictionary, 10th Edition, Online Version at http://v ww.m-w.com/. Claim 13 has also been modified for larity to recite "the central domai " It is believed that this amendment overcomes the rejectio .

As recited in amended claims 9, 12 and 13, and new c ims 24 - 27, the term "the corresp nding wild-type Begomovirus transcription activator prot n" refers to the un-modified, wild-ty e protein encoded by the non-mutated form of the AL2 g ne or gene fragment used to prepar the isolated recombinant polynucleotide. Applicant ubmits that the term "the corresp nding wild-type transcription activator protein" is clear n its meaning, and that the rejecti should be withdrawn.

Claim ejections - 35 USC § 112, first paragraph, written Descript n

Claims 7-9, 12, 13, 17, 18, 20 and 23 have been rejected un er §112, first paragraph.

The Patent Office has stated that no "description [is] giv n of what the corresponding wild-t e protein is," as recited in amended claim 7, and clai s 9, 12 and 13. Applicant respec ully disagrees with the Patent Office. The mutant protein recited in the pending claims are m ified forms of wild-type Begomoviral transcription activa r proteins. Figure 1 lists the amino cid sequences for the transcription activator proteins enco d by the AL2 genes from 13 differe t strains of Begomoviruses (a genus in the family of Ge iniviruses); Table 1 lists the GenB k accession numbers for the AL2 gene sequences om 70 different strains of

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Geminiviruses, most which are in the genus of Begomoviruses. Each one of t sequences so provided is a wild-ty sequence, as indicated in the specification at page 3, lin 2-3. Thus, in any comparison betw n mutant and wild-type forms of protein in each of the ins nt claims 7, 9, 12, and 13, and new claims 24 and 25, Applicant submits that ample inform tion has been provided to identify and describe wild-type transcription activator pr ins and the polynucleotides whic encode them. The recitation in the instant claims, as ended, of an "isolated recombinan polynucleotide that encodes a mutant Begomovirus transc tion activator protein, wherein said ecombinant polynucleotide is a modified open reading fra e of a selected wild-type AL2 gene om a Begomovirus strain," encompasses mutant forms of L2 genes from any Begomovirus. U on reading the specification, one of ordinary skill woul know that the "selected wild-type AL2 gene" recited in amended claim 7, and in claims 9, , 13, 24 - 27, encodes the non-mut ed, wild-type form of the Begomoviral transcription acti tor, and is the template from which e claimed modified isolated recombinant polynucleotide i lerived.

Specifically i regard to claims 7, 8, 9, 12 and 13, the Patent Office as stated that "[t]here is no struct ral description of what comprises the modified transcr tion activator protein ... [and] there is no description of the structural features that define the ge us" of claimed sequences. Applican respectfully disagrees.

The mutant p tein is a modified form of the highly conserved Geminivi s transcription activator protein ("T AP") encoded by the AL2 gene. Applicant has disclos the structural properties of the wil type AL2 transcription activator protein ("TrAP"), includi ; its molecular weight (15 kDa), an has provided information about its discrete domains an corresponding amino acid sequenc positions (see specification in PCT publication of International Application WO 99/63054, page 2, lines 25-35). Applicant has provided the wild-type seq nces for TrAP from a number of different Geminivirus strains, including those in the genus Begomovirus (see Figure 1, and SEQ ID NOs 1-13), as well as the wild-type polynucleotid sequences for AL2 from 70 differe t Geminivirus strains, including those in the genus of B omovirus (see Table 1, and SEQ ID NOs 76-147).

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Applicant has described sp cific mutations that are made in the context of the conserved wild-type TrAP protein sequence. In particular, Applicant has disclosed that modifications re made in the regions of a wild-typ Begomovirus AL2 polynucleotide which encode the aci ic and cysteine-histidine domains of rAP (see page 7, lines 10 and 11), and has identified how he mutations affect both the structur and the function of the mutant protein as compared to wi d-type (see pages 7-9). Applicant l as stated that substitutions, insertions and deletions are to be made in the context of specific co ons (i.e., deletions are made in increments of three nucleoti es to affect a modified protein lackin an amino acid corresponding to the position of the deletio a). (See specification, page 7, lines 13-14, page 8, lines 1-2 and 21-30.) Since insertions nd deletions are based upon discret amino acids, the size of the polynucleotide mutants nd resulting proteins could be readily calculated by one of ordinary skill.

Applicant has described d etions, insertions and substitutions in the AL2 polynucleot de sequence encoding the acidic do ain. Several examples of possible mutations are provid d, including substitution of one or r ore of the hydrophobic or acidic amino acids in the narr w range of amino acid positions 83- 29 (such as the conserved wild-type amino acids at positi ns 119 (isoleucine), or 123 (phenylal nine), or 124 (tryptophan) or 128 (phenylalanine)) with eit er small or non-charged amino acid , such as alanine or glycine. (See page 7, lines 1-3, page 8, lines 2-4 and lines 8-13.) App icant has likewise described modifications in the cystei e-histidine domain. For example, AL2 polynucleotide mutants have been described wher in several codons in the wild type op n reading frame encoding the central domain are deleted. As compared to TrAP wild-type, th encoded mutant protein lacks several amino acids in he specific range of amino acid positions 23-43. In yet another example, polynucleot de substitutions in the wild type op reading frame encode a mutant protein in which one or ve of the conserved wild-type TrAP ysteine or a combination of the cysteine and histidine resid es at amino acid positions 33-43 ar replaced with amino acids other than cysteine, histidine or methionine, such as glycine or al nine. (See page 8, lines 26-28). One specific example of a substitution in the cysteine-histidi e domain is the substitution of the histidine located at posit on 40 in the wild type protein with gl cine or alanine.

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The above examples reflect just a portion of the description which Applicant has provided regarding structural features of the mutant Begomovirus transcription activator protein recited in amended claim 7. With all of this detail regarding the structure of specific forms of mutant Begomovirus transcription activator protein, one skilled in the relevant art would surely recognize that Applicant had possession of the claimed invention at the time the application was filed. For all of the foregoing reasons, Applicant submits that claim 7 and all of its dependent claims 8, 9, 12, 13, 17, 18, 20 and 23, including new claims 24 - 27, are fully supported by the written description. Applicant respectfully requests withdrawal of the rejection of these claims.

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

Claims 7-9, 12, 13, 17, 18, 20 and 23 have been rejected under §112, first paragraph, as not enabled "for the reasons of record set forth in the last Office action." The Patent Office has stated that

> Applicant describes generally how to construct double domain genes having the desired characteristics, but does not teach specific mutations or give SEQ ID Nos for such constructs. Applicant claims mutation without reciting specific regions and specific domains ... and recites changes re 'the corresponding wild-type transcription activator protein' without defining what the wild-type transcription activator protein is. Since the double domain genes are not exemplified, the method of preparing a transgenic plant by using them is not enabled.

Applicant respectfully disagrees with the Patent Office. As recited in claim 7, the isolated recombinant AL2 polynucleotide comprises mutations in two specific regions of an AL2 gene sequence. Those regions are designated in the claim as corresponding to amino acids 83-129 and 23-43 of the encoded transcription activator, and represent the acidic and cysteine-histadine domains of the protein, respectively. Thus, the claim does not recite merely "any mutation" in "any" region. Further, as recited in claim 7, the resultant expression product is a modified transcription activator which is encoded by the mutant AL2 polynucleotide, not just "any modified transcription activator protein."

Applicant has done more than describe generally how to construct mutant AL2 polynucleotides as recited in amended claim 7; Applicant has identified specific locations for

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mutations, and has taught specific mutations using specific primer construct sequences. (See example 21 and Figure 2.) Applicant has described how to prepare mutants using known techniques, including PCR and site directed mutagenesis. (See page 9, and examples 22 and 23.) Applicant has provided an example of one possible mutation in the cysteine-histidine domain comprising substitutions at amino acid positions 33, 35, 40, and 43, wherein the cysteine and histidine residues found at those positions in the wild type form of TRAP are replaced with alanine (see specification at page 16, lines 10-3 and page 17, lines 1-14). In yet another example, Applicant has provided one possible combination of double domain mutations in which the resultant mutant form of TRAP lacks the amino acids which are found at acidic domain positions 115-129, and cysteine-histidine domain positions 33-43 in the wild type form of TRAP (see specification, page 20 lines 32-33 and page 21 lines 1-16.

As described above, Applicant has described the structural features of AL2 and its gene product, and has provided a multitude of examples of different wild-type forms of AL2, along with sequence information (see Table 1, and SEQ ID NOs 76-147). Applicant has also described that the mutant TrAP, in contrast to the wild-type protein, has diminished function, including reduced ability to bind to the native plant cell protein SNF-1 kinase, and reduced ability to activate transcription of critical viral genes. The mutant protein can thus confer to a transgenic plant expressing the protein a heightened resistance to Geminiviral infection. Applicant has specifically provided guidance as to which sites, which mutations, which deletions, and of what size, and which combinations of mutations, will provide such a mutant protein.

With all of the guidance and working examples of recombinant polynucleotides provided by Applicant, one of ordinary skill in the art would not have to conduct undue experimentation to practice the claimed invention. With the extensive guidance regarding Begomoviral AL2 genes and the encoded TrAP protein, as well as the specific mutations that may be made in each of the recited regions, and the specific primer constructs, one of ordinary skill could identify and select an AL2 gene to from which to derive the isolated recombinant polynucleotides recited in claim 7 and its dependent claims. One could then use known techniques, as well as the variety of different primer constructs provided by Applicant to prepare a modified transcription activator protein having mutations in both its c-terminal and central region domains, as recited in claim 7

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and its dependent claims. Accordingly, Applicant submits that claim 7 and its depended claims are enabled, and respectfully requests withdrawal of the rejection.

Claim Rejections - 35 USC § 102 (b)

Claims 7-9, 12, 13, 17, 18, 20 and 23 have been rejected under §102 (b), over applicant's admitted state of prior art.

The Patent Office has stated that the admitted prior art, Hamilton, et. al., (EMBO J. 3, 2197-2205, 1984) and Wu, et. al., (Phytopathology 86, 608-613, 1996) anticipates the claimed invention. More particularly, the Patent Office has stated that Hamilton and Wu each teach certain of the amino acid sequences listed in Figure 1 of the specification. Applicant respectfully disagrees with these statements, and further submits that Figure 1 does not disclose or embody Applicant's invention. Thus, even if either of the cited prior art references did teach the sequences in Figure 1, it would not follow that such reference anticipates any of the inventions recited in the instant claims.

Figure 1 provides aligned amino acid sequences of TrAP proteins encoded by wild-type AL2 genes from various Geminiviruses, including those in the genus of Begomoviruses. Neither Hamilton nor Wu discloses or teaches any amino acid sequence information for TrAP, or for any protein encoded by AL2. Hamilton provides data regarding the structural organization of genes in TGMV (a particular Geminivirus), and describes the putative multiple open reading frames for the TGMV genome. Wu provides polynucleotide sequences for the genome of AbMV, another Geminivirus. In regard to AL2, the most these references provide is polynucleotide sequence information for wild type AL2 genes in the Geminiviruses TGMV and AbMV. The amino acid sequence for the wild-type AL2-encoded TrAP form each of these two Geminiviral strains is included in Applicant's Figure 1, and corresponds with SEQ ID NOs 1 and 2.

Nowhere does either Hamilton or Wu disclose any AL2 polynucleotides having any mutations, much less recombinant AL2 polynucleotides having at least two mutations located in the specific regions as recited in amended claim 7, and its dependent claims 8,9, 12 and 13. Neither of these references discloses or even suggests modified forms of TrAP or AL2 gene

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ducts made using recombinant AL2 polynucleotide mut s. Nowhere does either Hamilton Wu disclose any vectors comprising such polynucleotide as recited in claims 17 and 18; or transgenic plants comprising such polynucleotides as re ed in claim 20; or any methods for king transgenic plants comprising such polynucleotides recited in claim 23. Lacking such closure, neither Hamilton nor Wu anticipates amended cl m 7 or any of its dependent claims, amended.

The Patent Office has stated that "the amino acid seq ence of the TGMV AL2 protein, as gned with the AL2 protein of AbMV is clearly mutant ne with the other," suggesting that milton and Wu teach mutant forms of the AL2 protein. Applicant respectfully submits that Patent Office has mischaracterized as "mutation" the known sequence variation that is served between wild type strains. As described in the s ecification, the AL2 gene is highly nserved among Geminiviruses, particularly Begomoviruse (see page 2, lines 25-35). It is well own in the art that there is always some variation betwe n the wild type gene sequences of ferent species or strains, even in the case of highly co served genes. Sequence variation tween wild-type TrAP proteins from different Geminivir s strains is evident in Figure 1, and Q ID NOs 1-13. The wild-type proteins listed in F ure 1, including those sequences closed by Hamilton and Wu, are not mutant forms o TrAP, and Applicant respectfully omits that one of ordinary skill in the art would not cons ler them to be mutant forms merely cause of some TrAP sequence variation between the Beg moviral strains. The term "mutant" used herein refers to variation in sequence that is the resul of deliberate genetic manipulation.

The sequence variation noted by the Patent Office between TGMV and AbMV is not esent in the most highly conserved portions of the AL2 g e products, namely amino acids 23- and 83-129 (see Figure 1); the very few sequence variat ns found in these highly conserved gions represent conservative amino acid substitutions. In contrast, the mutant forms of TrAP ade according to Applicant's invention in all cases call r non-conservative substitutions in se highly-conserved regions. Mutant proteins made acc ding to Applicant's invention using elected wild-type AL2 gene from one Begomoviral strain would not have the same amino acid quence as a wild-type TrAP protein from a different Beg moviral strain. Accordingly, while u and Hamilton each disclose wild-type AL2 gene sequer es having some sequence variation,

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the highly-co erved regions do not show variation other than wo t be achieved with conservative a no acid substitutions. Moreover, there is nothing in eithe Hamilton or Wu that even suggests utations in any form, much less the non-conservative su titutions in the most highly conser l portions of TrAP, as recited in claims 7-9, 12, 13, 17, 18, 0, 23, and 24-27.

For the easons given above, Applicant submits that neither Hamil n nor Wu anticipates any of claims -9, 12, 13, 17, 18, 20, 23, and 24-27. Accordingly, pplicant respectfully requests withd wal of the rejection of these claims.

New Claims 2

New cl ms 24- 27 recite various combinations of specific types or cations of mutations in the cysteine istidine and acidic domains of TrAP. Support for these laims is found in the original claim and in the specification, including the examples. Applic nt submits that these claims do not id new material and are free from the prior art for the r sons given above in connection wi claims 7-9, 12, 13, 17, 18, 20 and 23.

In view of the above-described amendments and remarks, it is sub itted that claims 7-9, 12, 13, 17, 18, 0, 23 and 24-27 are in condition for allowance. Prompt n ce of such allowance is respectfully quested.

Respectfully submitted,

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